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FACSIMILE TRANSMISSION SHEET

TO	Gailene Gabel
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FAX NO.	571-273-0820
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FROM: Jeffrey S. Sharp **EXTENSION:** 578
PAGES (INCLUDING THIS PAGE): **CLIENT NO:** 28911
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MESSAGE: Dear Examiner Gabel:

In preparation for our telephonic interview at 11 am EDT Tuesday please find attached an interview outline. I have also attached for easy reference copies of two exemplary claims.

If you have any questions or do not receive the entire fax please call me at 312-474-9578.

I will call you at your office at 11.

Regards

Jeff Sharp

Please contact Jeff Sharp at (312) 312-474-9578 if you do not receive all of the pages in good condition.

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TELEPHONIC INTERVIEW OUTLINE
USSN 09/027,654
Horton "IN-SITU EXTRACTION AND ASSAY METHOD"
11:00 a.m. EDT Tuesday, June 8, 2004
Examiner Gailene Gabel 571-272-0820

1. APPLICANT'S INVENTION

a. The present invention is directed to specific binding assays in which the presence of an intracellular analyte in a sample is assayed for by steps including reaction of a specific binding partner for the analyte with the analyte to form a specific binding partner-analyte complex and detection of that complex. (e.g., antigens and antibodies)

b. More particularly, the method of the invention includes the steps of mixing a sample of cells with a cell lysis agent to provide a lysed cellular sample, mixing the lysed cellular sample with a cyclodextrin sequestrant for the cell lysis reagent, and performing the specific binding assay in the presence of that sequestrant. The purpose of the sequestrant is to prevent the cell lysis reagent from adversely affecting the binding reaction between the analyte and its specific binding partner.

2. OUTSTANDING REJECTIONS

a. Claims 1-2, 4-5, 8, 10, 14 and 16-20 stand rejected under 35 U.S.C. §103 (a) as being obvious over Lundin, U.S. Patent No. 5,558,986 in view of the Khanna U.S. Patent No. 5,032,503.

b. Claims 6 and 9 stand rejected under 35 U.S.C. §103 (a) as being obvious over Lundin in view of the Khanna and in further view of Cook (2) WO 94/26413.

c. Claims 7 and 11-13 stand rejected under 35 U.S.C. §103(a) over Lundin in view of Khanna and further in view of Brown, U.S. Patent No. 5,739,001.

d. Claim 21 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Lundin, in view of Khanna, and further in view of Edmonds, U.S. Patent 6,159,750.

e. Claims 17 and 19 stand objected to as being substantial duplicates of one another.

3. PATENTABILITY ARGUMENTS

a. The Cited References:

Lundin is directed to enzyme mediated amplification assays in which a cyclodextrin is used as a sequestrant for a cell lysis reagent. Typical enzyme-mediated reactions include firefly luciferase assays, polymerase chain reaction (PCR) nucleic acid amplification, and restriction enzyme digestions in which an enzyme-mediated reaction amplifies the record of the presence of the involved enzyme through the catalysis of the enzymatic reaction to produce a product. Because an enzyme is not consumed in a catalytic reaction the reaction will continue and product will be produced until the reactants are exhausted.

Khanna is directed to specific binding assays in which cyclodextrin is used to neutralize the surfactant interference with specific binding pair interaction caused by the presence of low levels of detergent used to keep normally interacting components of a specific binding pair apart in a single liquid reagent. Khanna teaches away from the use of detergent levels sufficient to lyse cell samples and prescribes the use of low concentrations of surfactant (i.e., "[d]esirably, the concentration [of surfactant] will be insufficient to denature the specific binding pair members the sample analyte or any other assay reagents." (col. 4, lines 8-11).

Brown is directed to the use of a specific binding assay in a single reaction vessel.

Edmonds discloses a specific binding assay using fluorescence polarization assay.

Cook(2) WO 94/26413 relates to multiwell scintillation assays but teaches away from cell lysis with a detergent.

b. History of the Prosecution:

The claims of the application were originally rejected over the Lundin patent but those rejections were withdrawn in light of the Declaration of Dr. Horton filed October 22, 2001 and arguments to the effect that:

> one of ordinary skill in the art ... would not have expected the use of a cyclodextrin sequestering agent in the enzyme-mediated amplification assays of Lundin to be of benefit in a specific binding-type assay of the invention... (Response filed October 22, 2001)

More recently, the claims were rejected as being anticipated under 35 U.S.C. §102 by Khanna. Those rejections were withdrawn as a result of arguments that Khanna did not inherently anticipate the invention's cell lysis step because it used insufficient levels of detergent to cause cell lysis and did not teach i) carrying out a cell lysis step and ii) mixing and reacting the lysed sample with a specific binding assay reagent for an intracellular assay and to mix the lysed cellular sample with a cyclodextrin sequestrant for the cell lysis reagent.

Invention Discovery * whether an SBP can be performed using cyclodextrin

Currently, the claims are rejected based on the combination of Lundin and Khanna on the grounds that "it would have been obvious... to perform a specific binding assay as taught by Khanna on the intracellular analyte extracted from the lysed sample of Lundin because both of Lundin and Khanna use cyclodextrin to neutralize the effect of a detergent..."

c. Patentability Arguments:

The current rejection is flawed because the references fail to teach that cyclodextrin can neutralize the effects of detergent on a specific binding assay when the detergent is so strong that it can lyse cell samples. Specifically:

(1) Khanna should be the primary reference as it alone is directed to a specific binding assay but it does not teach the use of high levels of detergent

(2) Lundin which is directed to enzyme amplification assays does not teach that cyclodextrin can neutralize the effects of detergent on much more sensitive specific binding assays when the detergent is so strong that it can lyse cell samples.

(3) The Horton Declaration (October 22, 2001) demonstrates the significant differences between (a) an enzyme mediated assay in which even a small amount of un-neutralized enzyme can amplify a signal over time versus (b) a specific binding assay in which the amount of specific binding partner-analyte complex "product" produced will be limited to the amount of biologically active analyte.

(4) Lundin fails as a primary reference because it is directed to enzyme mediated amplification assays and not specific binding assays.

(5) Khanna does not rehabilitate Lundin as a primary reference because there is nothing in Khanna that teaches the success of cyclodextrin in neutralizing the effect of a detergent on a specific binding assay when the detergent is sufficient to lyse cellular samples.

EXEMPLARY CURRENT CLAIMS

1. [FIVE TIMES AMENDED] An improved method of conducting a specific binding assay for the presence of an intracellular analyte in a cultured cell sample which method comprises the steps of:

i) mixing a sample of cultured cells with a cell lysis reagent to provide a lysed cellular sample;

ii) mixing and reacting the lysed cellular sample with a specific binding assay reagent comprising a specific binding partner of the intracellular analyte and a tracer to perform a specific binding assay; thus forming a reaction mixture-comprising a specific-binding partner-intracellular analyte complex;

iii) mixing the lysed cellular sample with a cyclodextrin sequestrant for the cell lysis reagent, whereby the specific binding assay of step ii) is performed in the presence of the sequestrant; and

iv) detecting the presence of the specific binding partner-intracellular analyte complex, the presence of which is indicative of the presence of intracellular analyte in the sample wherein the improvement lies in the sequestrant preventing the cell lysis reagent from adversely affecting a binding reaction between the analyte and its specific binding partner.

14. [TWICE AMENDED] A kit, suitable for assaying for an analyte by the method as claimed in claim 17 comprising: a detergent; a sequestrant for the detergent; a specific binding partner of the analyte; a tracer; and separation means for separating bound tracer from unbound tracer.